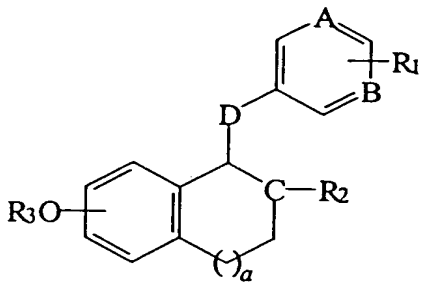
CLAIMS

1. A compound having the structure:



and stereoisomers and pharmaceutically acceptable salts thereof;

wherein

a is 0, 1 or 2;

A, B and C are independently CH, CR or N;

D is $-(CH_2)_r-$ or $-(CH_2)_nC(=O)(CH_2)_m-$;

R_1 represents one or two substituents independently selected from -X-Y;

R_2 is C_{1-8}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, $-C(=O)R_5$, a five- or six-membered heterocycle or heterocyclealkyl containing up to two heteroatoms selected from O, NR_c and $S(O)_q$, or a bicyclic ring system contain a five- or six-membered heterocycle fused to phenyl, wherein each of the above groups are optionally substituted with one to three substituents independently selected from -X-Y or R_4; and

R_3 is hydrogen, $-R_6$, $-(CH_2)_sC(=O)R_6$, $-(CH_2)_sC(=O)OR_6$, $-(CH_2)_sC(=O)NR_6R_7$, $-(CH_2)_sC(=O)NR_6(CH_2)_nC(=O)R_7R_8$, $-(CH_2)_sNR_6C(=O)R_7$, $-(CH_2)_sNR_6C(=O)NR_7R_8$, $-(CH_2)_sNR_6R_7$, $-(CH_2)_sOR_6$, $-(CH_2)_sSO_qR_6$ or $-(CH_2)_sSO_2NR_6R_7$;

and wherein

R_4 is at each occurrence independently halogen, hydroxy, carboxy, C_{1-6}alkyl, C_{1-4}alkoxy, C_{1-4}haloalkyl, C_{1-4}acyloxy, C_{1-4}thio, C_{1-4}alkylsulfinyl, C_{1-4}alkylsulfonyl, (hydroxy)C_{1-4}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, -C(=O)OH, -C(=O)OR, -OC(=O)R, -C(=O)NHR, -C(=O)NRR, -C(=O)NHOR, $-SO_2NHR$, $-NHSO_2R$, -CN, $-NO_2$, $-NH_2$, C_{1-4}alkylamino,

C_{1-4}dialkylamino, -NHC(=O)R, NHC(=O)$(CH_2)_s$(five- or six-membered heterocycle), a five- or six-membered heterocycle, or a five- or six-membered heterocycle fused to phenyl;

R_5, R_6, R_7 and R_8 are at each occurrence independently hydrogen, C_{1-8}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, or a five- or six-membered heterocycle or heterocyclealkyl containing up to two heteroatoms selected from O, NR_c and $S(O)_q$, wherein each of the above groups are optionally substituted with one to three substituents independently selected from R_4;

X is at each occurrence independently

a direct bond;

$-(CH_2)_nZ(CH_2)_m-$;

$-O(CH_2)_nZ(CH_2)_m-$;

$-S(CH_2)_nZ(CH_2)_m-$;

$-NR_c(CH_2)_nZ(CH_2)_m-$;

$-O(CH_2)_nCR_aR_b-$;

$-NR_c(CH_2)_nCR_aR_b-$;

$-OCHR_cCHR_d-$; or

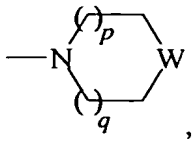
$-SCHR_cCHR_d-$;

Y is at each occurrence independently

halogen;

$-R_e$;

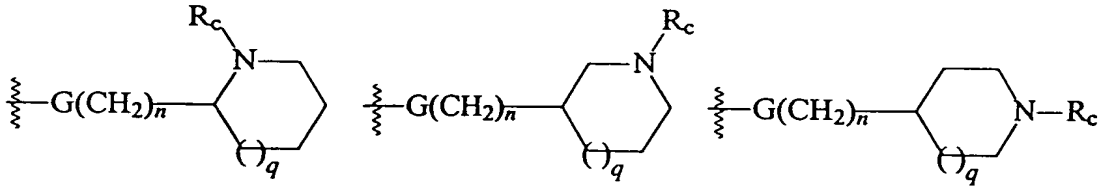
$-NR_eR_f$;

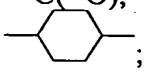


, optionally fused on adjacent carbon atoms with one or two phenyl or cycloalkyl rings, and with each carbon optionally and independently substituted with carbonyl or with one or two substituents independently selected from R_4, with any two R_4 substituents on a single carbon atom optionally being taken together to form a five- or six-membered heterocycle, and with each nitrogen atom

optionally and independently substituted with R_4, wherein W is $-NR_e-$, -O-, -S- or $-CR_eR_f-$; or a bridged or fused C_{5-12}bicyclic amine optionally substituted with one to three substituents independently selected from R_4;

or where -X-Y is



Z is CH_2, CH=CH, C≡C, O, NR_c, $S(O)_q$, C(=O), $C(OH)R_c$, $C(=O)NR_c$, $NR_cC(=O)$, $C(=O)NR_c$, $NR_cC(=O)$ or  ;

G is O, S or NR_e;

n and *m* are at each occurrence independently 0, 1, 2 or 3;

p is at each occurrence independently 1, 2 or 3;

q is at each occurrence independently 0, 1 or 2;

r is at each occurrence independently 1, 2, 3, 4 or 5;

s is at each occurrence independently 0, 1, 2, 3 or 4;

R is at each occurrence independently C_{1-6}alkyl;

R_a and R_b are at each occurrence independently C_{1-8}alkyl or taken together form a C_{3-8}cyclic alkyl;

R_c and R_d are at each occurrence independently hydrogen or C_{1-4}alkyl; and

R_e and R_f are at each occurrence independently hydrogen, C_{6-12}aryl, C_{1-8}alkyl, C_{7-12}aralkyl, a five- or six-membered heterocycle, or a five- or six-membered heterocycle fused to phenyl; or wherein R_e or R_f form a 3-8 membered nitrogen-containing heterocyclic alkyl with R_a or R_b; and wherein each R_e and R_f are optionally substituted with up to three substituents independently selected from R_4.

2. The compound of claim 1 wherein *a* is 1.

3. The compound of claim 1 wherein *a* is 0.

4. The compound of claim 1 wherein *a* is 2.

5. The compound of claim 1 wherein A and B are CH.

6. The compound of claim 1 wherein A is CH and B is CR.

7. The compound of claim 1 wherein A is CH and B is nitrogen

8. The compound of claim 1 wherein A and B are nitrogen.

9. The compound of claim 1 wherein C is nitrogen.

10. The compound of claim 1 wherein C is CH or CR.

11. The compound of claim 1 wherein D is $-(CH_2)_r-$.

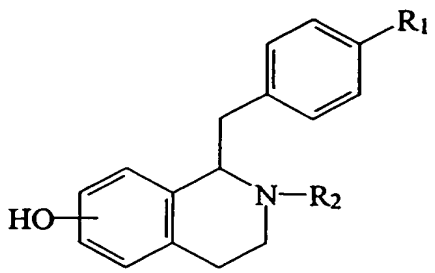
12. The compound of claim 11 wherien *r* is 1.

13. The compound of claim 1 wherein D is $-(CH_2)_nC(=O)(CH_2)_m-$.

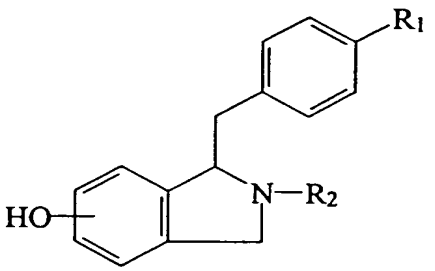
14. The compound of claim 13 wherein *n* and *m* are both 0.

15. The compound of claim 1 wherein A and B are CH, C is N and D is $-CH_2-$.

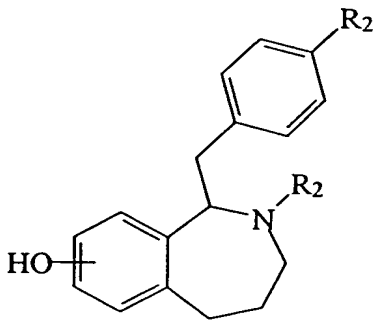
16. The compound of claim 15 wherein *a* is 1 and having the structure:



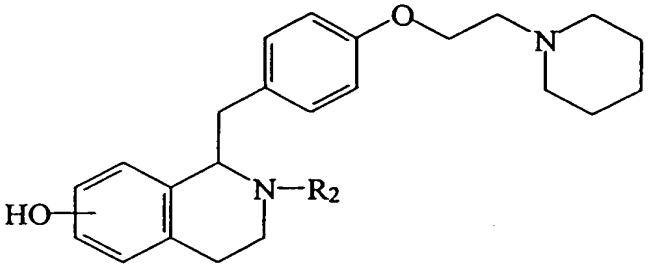
17. The compound of claim 15 wherein *a* is 0 and having the structure:



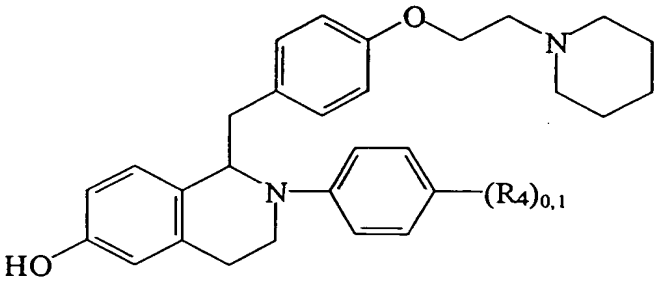
18. The compound of claim 15 wherein *a* is 2 and having the structure:



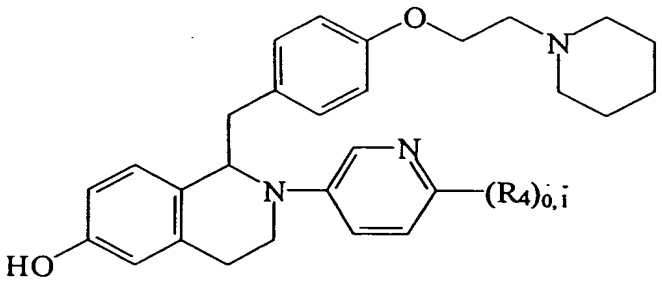
19. The compound of claim 16 having the structure:



20. The compound of claim 19 having the structure:



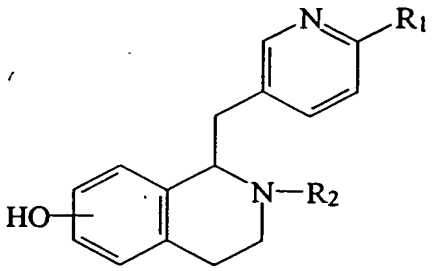
21. The compound of claim 19 having the structure:



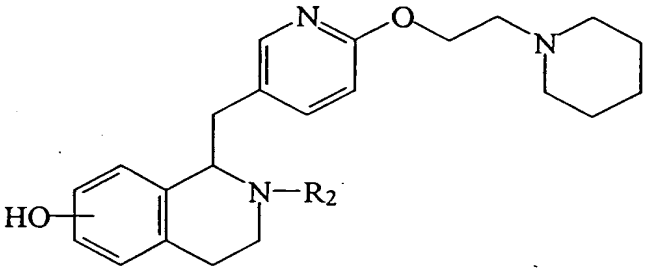
22. The compound of claim 19 wherein R_2 is $C_{1\text{-}8}$alkyl.

23. The compound of claim 1 wherein A is nitrogen, B is CH, C is nitrogen and D is $-CH_2-$.

24. The compound of claim 23 wherein *a* is 1 having the structure:



25. The compound of claim 24 having the structure:



26. The compound of claim 1 wherein A and B are N, C is N, and D is $-CH_2-$.

27. The compound of claim 1 wherein A, B and C are CH, and D is $-CH_2-$.

28. The compound of claim 1 wherein R_1 represents a single –X-Y substituent.

29. The compound of claim 28 wherein X is $-(CH_2)_nZ(CH_2)_m-$.

30. The compound of claim 29 wherein *n* is 0.

31. The compound of claim 30 wherein Z is oxygen.

32. The compound of claim 28 wherein X is a direct bond and Y is $-R_e$ or $-NR_eR_f$.

33. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier or diluent.

34. A method for modulating ER-β in a cell expressing ER-β, comprising contacting the cell with an effective amount of a compound of claim 1.

35. The method of claim 32 wherein the cell preferentially expresses ER-β over ER-α.

36. The method of claim 35 wherein the cell is of bone, bladder, uterus, ovary, prostate, testis, epididymis, gastrointestinal tract, kidney, breast, eye, heart, vessel wall, immune system, lung, pituitary, hippocampus or hypothalamus cell.

37. A method for modulating ER-β in tissue expressing ER-β, comprising contacting the tissue with an effective amount of a compound of claim 1.

38. The method of claim 37 wherein the tissue preferentially expresses ER-β over ER-α.

39. The method of claim 38 wherein the tissue is tissue of bone, bladder, uterus, ovary, prostate, testis, epididymis, gastrointestinal (GI) tract, kidney, breast, eye, heart, vessel wall, immune system, lung, pituitary, hippocampus or hypothalamus.

40. A method for treating an estrogen-related condition, comprising administering to an animal in need thereof an effective amount of a pharmaceutical composition of claim 33.

41. The method of claim 40 wherein the estrogen-related condition is breast cancer, osteoporosis, endometriosis, cardiovascular disease, hypercholesterolemia, prostatic hypertrophy, prostatic carcinomas, obesity, hot flashes, skin effects, mood swings,

memory loss, prostate cancer, menopausal syndromes, type-II diabetes, Alzheimer's disease, urinary incontinence, GI tract conditions, spermatogenesis, vascular protection after injury, endometriosis, learning and memory, CNS effects, plasma lipid levels, acne, hirsutism, solid cancers, multiple myeloma, lymphoma, hairloss, cataracts, natural hormonal imbalances, or adverse reproductive effects associated with exposure to environmental chemicals.

42. A method for inhibiting a cytokine in an animal in need thereof, comprising administering to the animal an effective amount of a compound of claim 1.

42. The method of claim 42 wherein the cytokine is IL-6

43. The method of claim 42 wherein the cytokine is GM-CSF.

44. A method for treating cancer associated with IL-6 in an animal in need thereof, comprising administering to the animal an effective amount of a compound of claim 1.